
MicroRNA regulation of cell lineages in mouse and human embryonic stem cells.

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Public Summary:

Scientific Abstract:

Cell fate decisions of pluripotent embryonic stem (ES) cells are dictated by activation and repression of lineage-specific genes. Numerous signaling and transcriptional networks progressively narrow and specify the potential of ES cells. Whether specific microRNAs help refine and limit gene expression and, thereby, could be used to manipulate ES cell differentiation has largely been unexplored. Here, we show that two serum response factor (SRF)-dependent muscle-specific microRNAs, miR-1 and miR-133, promote mesoderm formation from ES cells but have opposing functions during further differentiation into cardiac muscle progenitors. Furthermore, miR-1 and miR-133 were potent repressors of nonmuscle gene expression and cell fate during mouse and human ES cell differentiation. miR-1's effects were in part mediated by translational repression of the Notch ligand Delta-like 1 (DLL-1). Our findings indicate that muscle-specific miRNAs reinforce the silencing of nonmuscle genes during cell lineage commitment and suggest that miRNAs may have general utility in regulating cell-fate decisions from pluripotent ES cells.

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